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AB During mammalian ontogenesis, the thymic "pure" endodermal epithelial anlage develops and differentiates into a complex cellular microenvironment. Beginning the 7-8th week of intrauterine development, thymic epithelial cells chemotactically regulate (induce) numerous waves of migration of stem cells into the thymus, including the CD34+, yolk sac-derived, committed hematopoietic stem cells. In vitro experiments have established that CD34+ CD38dim human thymocytes differentiate into T lymphocytes when co-cultured with mouse fetal thymic organs. Hematopoietic stem cells for myeloid and thymic stromal dendritic cells (DCs) are present within the minute population of CD34+ progenitors within the mammalian thymus. The common myeloid, DC, natural killer (NK) and T lymphocyte progenitors have also been identified within the CD34+ stem cell population in the human thymus. Interactions between the endocrine and immune systems have been reported in various regions of the mammalian body including the anterior pituitary (AP), the skin, and the central (thymus) and peripheral lymphatic system. The network of bone marrow derived DCs is a part of the reticuloendothelial system (RES) and DCs represent the cellular mediators of these regulatory endocrine-immune interactions. Folliculo-stellate cells (FSC) in the AP, Langerhans cells (LCs) in the skin and lymphatic system, "veiled" cells, lympho-dendritic and interdigitating cells (IDCs) in a number of tissues comprising the lymphatic system are the cell types of the DC meshwork of "professional" antigen presenting cells (APCs). Most of these cells express the immunocytochemical markers S-100, CD1, CD45, CD54, F418, MHC class I and II antigens, Fc and complement receptors. FSCs are non-hormone secreting cells which communicate directly with hormone producing cells, a form of neuro-endocrine-immune regulation. As a result, an attenuation of secretory responses follows stimulation of these cells. FSCs are also the cells in the AP producing interleukin-6 (IL-6), and they have also been identified as the interferon-gamma responsive elements. FSCs also express lymphatic DC markers, such as DC specific aminopeptidase, leucyl-beta-naphthylaminidase, non-specific esterase, MHC class I and II molecules and various other lymphatic immunological determinants [platelet derived growth factor-alpha chain (PDGF-alpha chain), CD13, CD14 and L25 antigen]. There is strong evidence that such DCs in the AP, and similar ones in the developing thymus and peripheral lymphatic tissue are the components of a powerful "professional" antigen presenting DC network. These APCs contain a specialized late endocytic compartment, MIIC (MHC class II-enriched compartment), that harbors newly synthesized MHC class II antigens en route to the cell membrane. The limiting membrane of MIIC can fuse directly with the cell membrane, resulting in release of newly secreted intracellular MHC class II antigen containing vesicles (exosomes). DCs possess the ability to present foreign peptides complexed with the MHC molecules expressed on their surfaces to naive and resting T cells. There are a number of "molecular couples" that influence DC and T lymphocyte interaction during antigen presentation: CD1/CD18 integrins, intercellular adhesion molecules (ICAMs), lymphocyte function associated antigen 3 (LFA-3), CD40, CD80/B7-1, CD86/B7-2, and heat-stable antigen. The "molecular couples" are involved in adhesive or co-stimulatory regulations, mediating an effective binding of DCs to T lymphocytes and the stimulation of specific intercellular communications. DCs also provide all of the known co-stimulatory signals required for activation of unprimed T lymphocytes. It has been shown that DCs initiate several immune responses, such as the sensitization of MHC-restricted T lymphocytes, resistance to infections and neoplasms, rejection of organ transplants, and the formation of T-dependent antibodies. (ABSTRACT TRUNCATED)

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L5 ANSWER 1 OF 2 MEDLINE DUPLICATE 1

T1 Recycling MHC class I molecules and endosomal peptide loading.

AB MHC class I molecules usually present peptides derived from endogenous antigens that are bound in the endoplasmic reticulum. Loading of exogenous antigens on class I molecules, e.g., in cross-priming, sometimes occurs, but the intracellular location where interaction between the antigenic fragment and class I takes place is unclear. Here we show that measles virus F protein can be presented by class I in transporters associated with antigen processing-independent, NH(4)Cl-sensitive manner, suggesting that class I molecules are able to interact and bind antigen in acidic compartments, like class II molecules. Studies on intracellular transport of green fluorescent protein-tagged class I molecules in living cells confirmed that a small fraction of class I molecules indeed enters classical MHC class II compartments (MIICs) and is transported in MIICs back to the plasma membrane. Fractionation studies show that class I complexes in MIICs contain peptides. The pH in MIIC (around 5.0) is such that efficient peptide exchange can occur. We thus present evidence for a pathway for class I loading that is shared with class II molecules.

CT

Cell Membrane: PH, physiology

*Endoplasmic Reticulum: PH, physiology

*Endosomes: PH, physiology

HLA-D Antigens: PH, physiology

Herpesvirus 4, Human: GE, genetics

*Histocompatibility Antigens Class I: PH, physiology

Hydrogen-Ion Concentration

Kinetics

Luminescent Proteins: ME, metabolism

Measles Virus: IM, immunology

Recombinant Fusion Proteins: ME, . . .

CN 0 (HLA-D Antigens); 0 (Histocompatibility Antigens Class I); 0 (Luminescent Proteins); 0 (Recombinant Fusion Proteins); 0 (Viral Fusion Proteins)

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TITLE: Recycling MHC class I molecules and endosomal peptide loading.

AUTHOR: Gromme M; Uytendaele F G; Janssen H; Calafat J; van Binnendijk R S; Kenter M J; Tulp A; Verwoerd D; Neefjes J
CORPORATE SOURCE: Department of Tumor Biology, The Netherlands Cancer Institute, Plesmanlaan 121, 1066 CX Amsterdam, The Netherlands.

SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Aug 31) 96 (18) 10326-31. Journal code: PV3; 7505876. ISSN: 0027-8424.

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AB MHC class I molecules usually present peptides derived from endogenous antigens that are bound in the endoplasmic reticulum. Loading of exogenous antigens on class I molecules, e.g., in cross-priming, sometimes occurs, but the intracellular location where interaction between the antigenic fragment and class I takes place is unclear. Here we show that measles virus F protein can be presented by class I in transporters associated with antigen processing-independent, NH(4)Cl-sensitive manner, suggesting that class I molecules are able to interact and bind antigen in acidic compartments, like class II molecules. Studies on intracellular transport of green fluorescent protein-tagged class I molecules in living cells confirmed that a small fraction of class I molecules indeed enters classical MHC class II compartments (MIICs) and is transported in MIICs back to the plasma membrane. Fractionation studies show that class I complexes in MIICs contain peptides. The pH in MIIC (around 5.0) is such that efficient peptide exchange can occur. We thus present evidence for a pathway for class I loading that is shared with class II molecules.

L5 ANSWER 2 OF 2 MEDLINE DUPLICATE 2

AB . . . of "professional" antigen presenting cells (APCs). Most of these cells express the immunocytochemical markers S-100, CD1, CD45, CD54, F418, MHC class I and II antigens, Fc and complement receptors. FSCs are non-hormone secreting cells which communicate directly with hormone producing cells, a . . . as the interferon-gamma responsive elements. FSCs also express lymphatic DC markers, such as DC specific aminopeptidase, leucyl-beta-naphthylamidase, non-specific esterase, MHC class I and II molecules and various other lymphatic immunological determinants (platelet derived growth factor-alpha chain (PDGF-alpha chain), CD13, CD14 and L25. . . tissue are the components of a powerful "professional" antigen presenting DC network. These APCs contain a specialized late endocytic compartment, MIIC (MHC class II-enriched compartment), that harbors newly synthesized MHC class II antigens en route to the cell membrane. The limiting membrane of MIIC can fuse directly with the cell membrane, resulting in release of newly secreted intracellular MHC class II antigen containing vesicles. . .

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DOCUMENT NUMBER: 97437770 PubMed ID: 9292303

TITLE: Dendritic type, accessory cells within the mammalian thymic microenvironment. Antigen presentation in the dendritic neuro-endocrine-immune cellular network.

AUTHOR: Bodey B; Bodey B Jr; Kaiser H E

CORPORATE SOURCE: Department of Pathology, School of Medicine, University of Southern California, Los Angeles, USA.

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